REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Unity of Invention

The examiner has restricted the claims for unity of lack invention on the basis that Chiba reference anticipates the present invention. As discussed below, however, the Chiba reference does not disclose the present invention. Therefore, applicants respectfully request that the finding of lack of unity of invention be withdrawn and all of the claims be examined together.

Drawings

The Examiner has not yet indicated in the Office Action Summary that the formal drawings filed with the original application papers have been accepted. Acceptance of these drawings by checking the appropriate boxes in the Office Action Summary is respectfully requested in the next communication from the Examiner. ***This is the second request for acknowledgement that the drawings are accepted.***

Rejections Under 35 USC 112, First and Second Paragraphs

Applicants traverse the examiner's findings for lack of enablement and written description of the following reasons.

The examiner still asserts that the specification does not provide written description support or enablement for the present the present claims. The examiner does acknowledge that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure.

Applicants attach hereto a table (see Appendix I) summarizing origins, GenBank numbers, homologies, and relevant literature and is presented as evidence of enablement and written description of the claimed genes to be disrupted, genes to be introduced, and markers

used in preparation of a yeast mutant producing a glycoprotein having a mammalian-type sugar chain.

With respect to the genes to be disrupted, the genes having similar functions to that of MNN1, MNN4, and OCH1 genes are present in multiple species of yeasts, as shown in the attached sheet. In addition, it is understood that homology among genes having similar functions is generally high. That is, genes characterized by similar functions and structures are present in various species of yeast, as well as in Saccharomyces cerevisiae. Therefore, any kinds of yeasts having the functional characteristics of MNN1, MNN4, and OCH1 genes coupled with a known or disclosed correlation between function and structure can be used in the present invention. Saccharomyces cerevisiae is only a representative species of yeasts having the above characteristics.

Thus, applicants urge that a person skilled in the art would be able to predict and select the yeasts to be used in the present invention and carry out the invention. In fact, after the published date of the present application, it was reported that a glycoprotein containing a mammalian type sugar chain could be produced in another species of yeast, Pichia pastorsis, by the same technique as that of the present application. See Proc. Natl. Acad. Science 100, 5022-5027, 2003, and Nature Biotechnology, 210-215, 2006 (Appendix II).

Also, with respect to the genes to be introduced, genes having similar functions to those of a-mannosidase I and GnT-I genes are present in multiple species, as shown in the attached sheet. The amino acid sequences of α-mannosidase I and GnT-I derived from other species have at least 30% or more homology, and in particular, 80% or more homology in cases of the same genus, with those of α-mannosidase I derived from Aspergillus saitoi and rat GnT-I. Therefore the possibility that genes having similar functions would resemble each other in structure is high.

Therefore, applicants assertion that any yeasts and any genes derived from various species can be used, and that desirable results can be obtained when using any yeasts and any genes derived from various species, is supported by rational grounds based on functional characteristics coupled with a known or disclosed correlation between function and structure as described above. Therefore, applicants request the rejections for lack of written description and enablement be withdrawn.

Claim Rejections - 35 USC 102

The examiner maintains the rejection under 35 USC 102 (b) over Chiba et al., J. Biol. Chem., 273, pp. 26298-26304, 1998 ("Chiba et al.").

In order to overcome this rejection, applicants have amended claims 88 and 91 from "a polynucleotide encoding N-acetylglucosaminyl transferase-I" to "a polynucleotide that contains the ORF encoding-N-acetylglucosaminyl transferase-I." This is no description or suggestion with regard to expression of an intact GnT-I reading frame in Chiba et al.

The step of expressing the GnT-I gene, is novel and unobvious over Chiba et al. In Chiba et al., introduction of the GnT-I gene into host cells is not actually conducted. In fact, a reference to "an object of our future research" made on page 26303, right column, last line of Chiba et al., conversely suggests that further research was required for co-expression of alpha-1,2-mannosidase (α-mannosidase I) and GnT-I at the time of the published date of Chiba et al.

Moreover, in Yoshida et al., Glycobiology, 9, pp. 53-58, 1999 (reference C1 of the August 5, 2004 IDS), the GnT-I activity was confirmed only *in vitro* using oligosaccliarides (on page 56, right column, line 20 from the bottom). Yoshida et al. was cited as D2 in counterpart EP case, and a copy of the document is attached herewith. It could not have been expected that GnT-I activity *in vitro* is completely maintained *in vivo*, since the *in vivo* environment is very complicated compared with the *in vitro* environment, and activity *in vivo* is likely to be affected by various factors. In fact, Yoshida et al. states that, in A. nidulans, GnT-I is active *in vitro* but does not function *in vivo* (see page 56, left column, at lines 36 & 37).

On the other hand, in a yeast mutant of the present invention, in which the MNN1 gene, the MNN4 gene, and the OCH1 gene are disrupted, and into which are introduced a polynucleotide encoding α-mannosidase I and a polynucleotide that contains the open reading frame (ORF) encoding N-acetylglucosaminyl transferase-I, it is actually confirmed that the sugar chain of cell surface mannan-protein of the yeast is a hybrid-type sugar chain represented by formula (IV). In other words, GnT-I activity in a sugar chain of glycoprotein is confirmed *in vivo*. The result obtained in this application that a yeast mutant, wherein the MNN1 gene, the MNN4 gene, and the OCH1 gene are disrupted, and into which the α-mannosidase I gene and the GnT-I gene which comprises the ORF (the polynucleotide that

contains the ORF encoding N-acetylglucosaminyl transferase) introduced, is capable of producing a hybrid-type sugar chain *in vivo* is not described Chiba et al. and cannot be unreasonable unexpected from the teachings of Chiba et al. Therefore, the present application should not be rejected as being anticipated by Chiba et al. under 35 USC 102(b).

CONCLUSION

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By _____

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